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Hospital and 1-Year mortality Outcomes in COVID-19 pneumonia

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Abstract
Aim: COVID-19 caused many deaths, and its socioeconomic impact continues. Hospital mortality is generally known, but information on 1-year mortality is limited. This study aimed to measure all-cause mortality rates in hospitalized and 1-year follow-up COVID-19 patients and to evaluate the factors affecting these rates.
Material and Methods: PCR-positive patients' demographic, clinical, and laboratory characteristics were retrospectively analyzed. Hospitalization duration and mortality data were recorded. Discharged patients' polyclinic, follow-up, and mortality status within one-year were evaluated.
Results: The study included 201 patients, with a mean age of 63.12±14.5 years, and 59.2% were male. Logistic regression analysis identified several factors affecting hospital mortality, including male gender, smoking, lactate-dehydrogenase, and ferritin. Further analyses indicated that advanced age, low-oxygen saturation, high-sodium levels, low-potassium levels, low-hemoglobin), elevated-white-blood cell count, reduced-platelet count, increased INR and D-Dimer count, and elevated-CRP (C-reactive protein) levels were significant factors influencing hospital mortality. Mortality within 1-year was associated with factors including male gender, diabetes, low-oxygen saturation, elevated-AST levels, elevated-ALT levels, elevated-ferritin levels, and hospitalization length. Those who died within one year were more likely to have been hospitalized in intensive-care unit, required oxygen support, and were smokers.
Discussion: Hospital mortality was associated with impaired laboratory parameters and smoking, whereas 1-year mortality was associated with intensive-care, oxygen requirements, and diabetes.

Keywords
COVID-19, Mortality, Risk Factors, Pneumonia

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Introduction

Beginning as an outbreak in December in China, the so-called novel coronavirus 2019 has since spread rapidly worldwide. According to the World Health Organization (WHO), there are no specific drugs or antiviral therapies to treat or prevent the novel coronavirus. Studies show that one-year mortality is in one-third of discharged patients with pneumonia or acute respiratory distress syndrome who survive in the hospital [1,2]. Especially in covid-19 patients developing respiratory failure, there is a risk of mortality even if discharged from the hospital. Studies have shown that advanced age, male gender, comorbid cardiovascular diseases, diabetes, chronic obstructive pulmonary disease (COPD), and malignancies increase hospital mortality [3,]. Considering these premises, it seems reasonable to expect a significant long-term mortality rate after hospitalization in COVID-19 patients; however, little is known about post-discharge mortality, and scientific evidence is still limited[4]. Risk factors predicting this risk should be investigated more extensively. Awareness should be raised among physicians about the predictors of post-discharge mortality, and a follow-up program should be structured for discharged patients. In our study, patients' in-hospital and 1-year post-discharge mortality evaluations were performed more comprehensively with demographic, clinical, and laboratory data.

Material and Methods

Between May 2020 and July 2020, covid-19 pneumonia patients over the age of 18 who were PCR positive and followed up in the covid-19 pandemic service and intensive care unit of Van Yüzüncü Yıl University Faculty of Medicine Hospital were included in the study. Patient data (demographic, clinical, laboratory, and imaging) were obtained retrospectively from the files and hospital registration system. Patients aged below 18 years, those with negative PCR tests, pregnant women, and those with missing data in their files were excluded from the study. 1st-year survival of discharged patients was recorded by phone or through the system.

Statistical Analysis

Descriptive statistics for continuous variables were expressed as Mean, Standard Deviation, Minimum, and Maximum values, while descriptive statistics for categorical variables were expressed as numbers and percentages. One-way analysis of variance was used to compare group averages in terms of continuous variables. Pearson correlation coefficients were calculated to determine the relationship between these variables. Logistic regression analysis was also performed to determine the effect of categorical variables on survival. The statistical significance level was taken as 5%, and the SPSS (ver: 21) statistical package program was used for calculations.

Ethical Approval

The study was conducted in accordance with ethical rules.

Results

The mean age of the 201 patients in the study was 63.12±14.5 years (59.2% male). 59.2% (n:119) of the patients were hospitalized in non-intensive care units. The most common comorbidities were hypertension (41.3%) and diabetes (25.4%), COPD (21.9%), and asthma (8%). The number of patients who died in the hospital was 61 (30.3%), and the number of patients who died within one year after discharge was 15 (7.5%). According to logistic regression analysis, the factors affecting in-hospital mortality were male gender (OR:34.8 p=0.005), smoking (OR:7.6 p=0.007), lactate dehydrogenase (OR:1.01 p=0.003), and ferritin (OR:1 p=0.002) (Table 1). In additional analyses, high age (p=0.000), low oxygen saturation (p=0.000), high sodium (p=0.021), low potassium (p=0.013), low hemoglobin (p=0.003), elevated white blood cell count (p=0.000), low platelet count (p=0.008), elevated INR and D-Dimer (p=0.000), and elevated CRP (p=0.000) were found to be effective in-hospital mortality (Table 2). The presence of diabetes (OR: 18 p=0.053), low oxygen saturation (OR: 0.78 p=0.046), elevated AST (OR: 0.79 p=0.047), elevated ALT (OR: 1.04 p=0.049), elevated ferritin (OR: 1.007 p=0.013) and length of hospitalization (OR: 1.2 p=0.046) affected mortality within one year after discharge (Table 3). Patients who died within one year were hospitalized in the intensive care unit (p=0,000), received oxygen support (p=0,000), and most of them were smokers (p=0,000). Within one year, the causes of mortality were cardiovascular diseases (n:6), malignancy (n:2), and post-covid respiratory failure (n:6).

Discussion

COVID-19 remains a global problem for which there is no cure. Since there is no cure, controlling risk factors for the accompanying poor prognosis should be prioritized in these patients. Covid-19 is a viral infection, and the picture it creates is similar to pandemics and epidemics that existed in other times. Therefore, studies showing mortality risk factors in viral pneumonia over such a high number of patients will contribute to the literature.

In our study, it was noteworthy that the factors that triggered hospital mortality were primarily male gender, smoking, and laboratory parameters, while in 1-year mortality, intensive care unit hospitalization, oxygen requirement, and the presence of diabetes mellitus were additionally observed. While the overall hospital mortality rate is 5.2%, the mortality rate varies between 30% and 65% in patients who need mechanical ventilation or are hospitalized in the intensive care unit for advanced supportive treatment [5, 6]. Mortality rates changed in the first and second waves of Covid-19 [7].

The mutation of the virus and the ability of the health system to control patients and risk factors may be a factor in this. Our study was conducted during the first wave, and the hospital mortality rate was 30.3% (n:61). Although recent advances in treatment and the availability of vaccines have reduced mortality and morbidity due to COVID-19, the disease was characterized by high mortality in the early stages of the pandemic [8] .In another study, hospital mortality was found to be 31.1%, just like in our study[9].While the hospital mortality rate in our study was the same as in this study, the 1-year mortality rate was 7.5%. In this study, 1-year mortality was 3.3%(12). The higher 1-year mortality rate in our study may be because many patients were hospitalized in the intensive care unit. In the meta-analysis by Ramzi et al., the all-cause mortality rate after discharge, especially in COVID-19, was 7.5%[4].This result was similar to our study. In a study by Herridge et al., the one-year

mortality rate was 11% in ARDS survivors [10]. Interestingly, other longitudinal studies of ARDS survivors found advanced age and pre-ICU comorbidities as independent predictors of mortality rather than the severity of disease or ICU factors [11].The results of these studies were similar to our study. The variability in reported mortality rates may be explained by different treatment approaches between countries, differences in the number of beds and healthcare personnel in intensive care units, medical infrastructure, and follow-up periods [12]. When the literature is examined, although there are various limitations regarding the results obtained due to the number of patients, differences in study designs, and lack of data, many prognostic factors and conditions affecting mortality have been defined. Our study investigating the factors affecting mortality and morbidity in patients with COVID-19 showed that the age factor was significant, and male gender and the presence of comorbid diseases in 1-year mortality were also associated with a high mortality rate. When the relationship between SARS-CoV-2 and gender was investigated, it was reported that men were more frequently infected than women, and the likelihood of developing Acute Respiratory Distress Syndrome was higher in older men with comorbidities than women [12]. Although there have been animal experiments on patients with ARDS, there is no proven medicine currently in use [13]. A Chinese study found that among those with a disease picture, severe disease, and mortality rates were higher in men, especially in the 50-69 age group [14].In this study, in which data from ten European countries were evaluated, it was found that advanced age and male gender increased mortality. In our study, the mean age of those who died was 69± 13.2 years and p=0000. It was observed that the male gender had a 34 times higher mortality rate. It is thought that the low mortality rate in women may be due to hormonal reasons and immune response differences [15]. In Covid -19 patients, no association was found between hospital survival and one-year survival regarding asthma, COPD and hypertension, while a negative association was found between 1-year survival and diabetes mellitus. In hospital mortality, although not statistically significant, HT was associated with 1.3-fold COPD, 1.5-fold asthma 1.8-fold mortality. A study found that comorbid pathologies such as hypertension, hypercholesterolemia, heart disease, diabetes mellitus, malignancy, chronic obstructive pulmonary disease, chronic kidney disease, and medications used before hospitalization were associated with mortality [16]. Although Alhakak et al. [17] reported that diabetes was associated with mortality in more than 3000 patients, there

Table 1. Examination of risk factors affecting hospital mortality (logistic regression analysis)

	OR (95% CI)	p
Age (years)	1,0,60 (0,996-1,128)	0,064
Gender	34,862(2,981- 407,6)	0,005
BMI(%)	0,974(0,805 – 1,178)	0,785
Oxygen saturation	0,936 (0,866 – 1,011)	0,091
Glomerular filtration rate	0,998(0,979 – 1,017)	0,839
ALT	0,993(0,976-1,010)	0,419
AST	1,010(0,972-1,049)	0,61
LDH	1,010(1,003-1,017)	0,003
D-Dimer	1,190(0,814-1,739)	0,37
lymphocyte	0,963(0,804-1,153)	0,68
hemoglabin	0,805(0,602-1,0,76)	0,143
platelet	1,000(1,000-1,000)	0,239
Ferritin	1,002(1,001-1,004)	0,002
CRP	1,010(0,998-1,021)	0,093
Length of hospitalization(days)	0,932(0,825-1,053)	0,259
COPD	1,522 (0,402-5,75)	0,536
Asthma	1,806 (0,155-21,006)	0,637
Hypertension	1,320 (0,296-5,896)	0,716
Cigarette	7,664 (1,731-33,938)	0,007

Table 2. Descriptive statistics and ANOVA analysis of patients who survived and died in the hospital according to quantitative data

	Survived (SD±)	Ex	p
Age(years)	60,56±14,3	69±13,2	0
Body mass index (BMI)	28,01±4,5	27,2±3,3	0,245
Oxygen saturation(%)	87,23±6,1	82±6,1	0
Creatinine (mg/dl)	0,82±0,31	0,91±0,45	0,306
Glomerular filtration rate (GFR) (mL/min)	398±2603	102±54	0,402
ALT(IU/L)	55,89±57	98±251	0,06
AST(IU/L)	37,72±22,9	134 455	0,013
Sodium(mEq/L)	136±12	140±6,6	0,021
Potassium(mmol)	4,26±1,2	4,03±0,73	0,013
White sphere x 103 /mm³	8,3 ±3,2	18, 2± 27,1	0
Hemoglobin gr/dL	12,8 ±2,03	11,7± 2,6	0,003
Platelets /µL	267 ± 128	218 ±103	0,008
Lymphocytes x 103/µL	1,22± 0,74	3,3 ±16,6	0,13
Ferritin (ml/ng)	505 ± 411	3190± 7459	0
INR	1,02± 0,8	1,21± 0,35	0
D-Dimer (ng/mL)	1,38 ±1,7	5,4 ±7,3	0
C-Reactive Protein (CRP)(mg/L)	40,73± 46,3	94± 73,6	0
Length of hospitalization (Days)	1,09± 6,8	12,58 ±6,6	0,137

Table 3. Examination of risk factors affecting 1-year mortality (logistic regression analysis)

	OR (95% CI)	p
Age (years)	1,125 (0,950 – 1,333)	0,173
Gender	11,126 (0,121- 1027,2)	0,297
BMI(%)	0,754(0,304 – 1,873)	0,544
Oxygen saturation	0,781 (0,613 – 0,995)	0,046
Glomerular filtration rate	1,000(0,998 – 1,002)	0,9
ALT	1,048(1-1,098)	0,049
AST	0,795(0,634-0,699)	0,047
LDH	0,989(0,975-1,004)	0,149
Sodium	0,795(0,634-0,997)	0,324
White sphere	1,517(0,894-2,572)	0,122
hemoglabin	0,380(0,127-1,135)	0,083
platelet	1,000(1,000-1,000)	0,239
Ferritin	1,007(1,001-1,012)	0,013
CRP	1,007(0,971-1,046)	0,695
Length of hospitalization(days)	1,275(1,004-1,618)	0,046
Diabetes Mellitus	18,050(0,995-337,5)	0,053

is no data on 1-year mortality. In studies conducted with more patients in the literature, results were obtained that mortality increased in the presence of diabetes, malignancy, or three or more comorbidities [18]. Many studies show renal dysfunction is associated with poor prognosis and mortality[19].However, our study found no association between renal function and early or late mortality. When the relationship between acute phase reactants and mortality risk was analyzed, mortality risk increased 1-fold for each unit increase in CRP level, 1-fold for each 1 unit increase in ferritin level, 1-fold for each 1 unit decrease in lymphocyte level, and 1-fold for each 1 unit increase in LDH level. D-dimer, a marker of coagulation and inflammation, was found to be significantly higher in the deceased group compared to the survivors in the ANOVA test (p=0.000), but no statistical significance was found in the logistic regression analysis, a 1-fold increase in mortality was observed for each unit increase. Other studies in the literature have concluded that D-dimer and CRP may be important markers in monitoring disease activity [20]. In a meta-analysis, elevated serum CRP, procalcitonin, D-dimer, and ferritin levels were associated with severe disease, high mortality, ARDS, and increased need for intensive care [21]. Our study concluded that LDH, white blood cell, AST, ALT, platelet, D-dimer, CRP, ferritin, and INR levels among inflammatory markers were associated with mortality. In a cohort study by Henry et al., higher ferritin levels were found in patients who died, similar to our study [22]. In a meta-analysis conducted in China, it was emphasized that monitoring ferritin levels may be useful in recognizing patients who may have high mortality [23]. According to a study conducted in Wuhan, it was shown that patients with D-dimer levels higher than 2.0 ng mL-1 had a higher mortality rate than patients with values below 2.0 ng mL-1 [12]. The results prove that COVID-19 infection occurs with a coagulopathy problem that increases mortality characterized by procoagulant factors such as fibrinogen and high D-dimer levels [12]. In our study, similar to the literature, high ferritin and D-dimer levels increased mortality. In addition, low hemoglobin, low O2 saturation, and low electrolytes such as sodium and potassium were also found to be associated with mortality. In another study, hemoglobin levels below 11 g/dl were associated with disease progression in COVID-19 patients[24].A meta-analysis of a 2019 multicenter observational study of risk factors for disease progression in patients with mild to moderate coronavirus disease found results similar to those of our study[25].All assessments were based on hospital mortality. Data on 1-year mortality is limited.

Limitation

Due to the clinical and laboratory heterogeneity among the patient groups we compared, as well as the retrospective nature of our single-center study, it is important to note that our findings may not directly apply to other settings with different populations and case mixes.

Conclusion

Since there is no definitive cure for COVID-19, which poses a serious public health problem on a global scale, identifying the group of patients at risk for poor prognosis from the moment of admission is critical in managing the process. Awareness among physicians about post-discharge mortality predictors can help structure a follow-up program for discharged patients. Covid-19 is a viral infection, and the picture it creates is similar to pandemics and epidemics occurring at other times. Studies showing mortality risk factors in viral pneumonia over such a large number of patients will contribute to the literature.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or compareable ethical standards.

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Conflict of Interest

The authors declare that there is no conflict of interest.

References

1. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy region, Italy. JAMA. 2020;323(16):1574–1581.

2. Schmidt M. Clinical characteristics and day-90 outcomes of 4244 critically ill adults with COVID-19: A prospective cohort study. Intensive Care Med. 2020;47(1):60–73.

3. Parohan M, Yaghoubi S, Seraji A, Javanbakht MH, Sarraf P, Djalali M. Risk factors for mortality in patients with Coronavirus disease 2019 (COVID-19) infection: A systematic review and meta-analysis of observational studies. Aging Male. 2020;23(5):1416-24.

4. Ramzi ZS. Hospital readmissions and post-discharge all-cause mortality in COVID-19 recovered patients; A systematic review and meta-analysis. Am J Emerg Med. 2021;51(1):267–279.

5. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med 2020;180(7):934-43.

6. Baud D, Qi X, Nielsen-Saines K, Musso D, Pomar L, Favre G. Real estimates of mortality following COVID-19 infection. Lancet Infect Dis 2020;20(7):773.

7. Meschiari M, Cozzi A, Tonelli R, Bacca E, Menozzi M, Franceschini E, et al. First and second waves among hospitalised patients with COVID-19 with severe pneumonia: A comparison of 28-day mortality over the 1-year pandemic in a tertiary university hospital in Italy. BMJ Open. 2022;12(1):54-69.

8. Chang R, Elhusseiny KM, Yeh YC, Sun WZ. COVID-19 ICU and mechanical ventilation patient characteristics and outcomes-A systematic review and meta-analysis. PloS One 2021;16(2):246-318.

9. Novelli L, Raimondi F, Carioli G, Carabbio A, Papacena S, Biza R, et al. One-year mortality in COVID-19 is associated with patients' comorbidities rather than pneumonia severity. Respir Med Res. 2022;83(1):1-8.

10. Herridge MS, Cheung AM, Tansey CM, Matte-Martyn A, Diaz-Granados N, Al-Saidi F, et al. One-year outcomes in survivors of the acute respiratory distress syndrome. N Engl J Med. 2003;348(8):683–693.

11. Wang CY, Calfee CS, Paul DW, Janz DR, May AK, Zhuo H, et al. One-year mortality and predictors of death among hospital survivors of acute respiratory distress syndrome. Intensive Care Med. 2014;40(1):388–396.

12. Armstrong RA, Kane AD, Kursumovic E, Oglesby FC, Cook TM. Mortality in patients admitted to intensive care with COVID-19: An updated systematic review and meta-analysis of observational studies. Anaesthesia 2021;76(4):537-48.

13. Candaş A, Yucel B, Savaş MN. Proanthocyanidin reduces nitrogen mustard-induced lung injury. Gülhane Tıp Derg. 2008;50(4):267-72.

14. Conti P, Younes A. Coronavirus COV-19/SARS-CoV-2 affects women less than men: Clinical response to viral infection. J Biol Regul Homeost Agents 2020;34(2):339-43.

15. Pradhan A, Olsson PE. Sex differences in severity and mortality from COVID-19: Are males more vulnerable? Biol Sex Differ. 2020;11(1):53.

16. Grasselli G, Greco M, Zanella A, Albano G, Antonelli M,Bellani G, et al. Risk Factors Associated With Mortality Among Patients With COVID-19 in Intensive Care Units in Lombardy, Italy. Intern Med 2020;180(10):1345-55.

17. Alhakak A, Butt JH, Gerds TA, Mogensen MV, Kroll JPalligaard JL, et al. Glycated haemoglobin levels among 3295 hospitalized COVID-19 patients, with and without diabetes, and risk of severe infection, admission to an intensive care unit and all-cause mortality. Diabetes Obes Metab. 2022;24(3):499-510.

18. Ssentongo P, Ssentongo AE, Heilbrunn ES, Ba DM, Chinchilli VM. Association of cardiovascular disease and 10 other pre-existing comorbidities with COVID-19 mortality: A systematic review and meta-analysis. PLoS One. 2020;15(8):1-16.

19. Shao M, Li X, Liu F, Tian T, Luo J, Yang Y. Acute kidney injury is associated with severe infection and fatality in patients with COVID-19: A systematic review and meta-analysis of 40 studies and 24,527 patients. Pharmacol Res. 2020;161(1):105-107.

20. Valerio L, Ferrazzi P, Sacco C, Ruf W, Kucher N, Konstantinides SV, et al. Humanitas COVID-19 Task Force. Course of D-dimer and c-reactive protein levels in survivors and nonsurvivors with COVID-19 pneumonia: a retrospective analysis of 577 patients. ThrombHaemost. 2021;121(1):98-101.
21. Huang I, Pranata R, Lim MA, Oehadian A, Alisjahbana B. C-reactive protein, procalcitonin, D-dimer, and ferritin in severe coronavirus disease-2019: A meta-analysis. Ther Adv Respir Dis. 2020;14(2):1-14.
22. Henry BM, de Oliveira MHS, Benoit S, Plebani M, Lippi G. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): A meta-analysis. Clin Chem Lab Med 2020;58(7):1021-8.
23. Cheng L, Li H, Li L, Liu C, Yan S, Chen S, et al. Ferritin in the coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis. J Clin Lab Anal 2020;34(10):1-18.
24. Cen Y, Chen X, Shen Y, Zhang XH, Lei Y, Xu C, et al. Risk factors for disease progression in patients with mild to moderate coronavirus disease 2019-a multicenter observational study.Clin Microbiol Infect 2020;26(9):1242.
25. Kowsar R, Rahimi AM, Sroka M., Mansouri A, Sadeghi K, Bonakdar E, et al. Risk of mortality in COVID-19 patients: A meta-and network analysis. Scientific Reports, 2023;13(1):2138.

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